

De e. a leptin receptor as described in (a)-(d) above in which a cysteine is substituted with an amino acid selected from the group consisting of serine, threonine, and alanine;

wherein the numbering is based on the amino acid sequence of SEQ ID NO:84.

REMARKS

The foregoing amendments and the following remarks are submitted in connection with a response to the communication and Notice dated July 1, 2001. In particular, the above amendments are provided to enter reference to particular SEQ ID Nos: in the claims, as requested by the Examiner. The above amendments provide no new matter and are made in order to clarify the leptin receptors to which the claims refer.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,
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Version to Show Markings of Changes Made

30. (Three Times Amended) An oligonucleotide hybridizable under stringent conditions to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of:

a. a leptin receptor selected from the group consisting of OB-Ra (SEQ ID NO:2), OB-Rb (SEQ ID NO:4), OB-Rc (SEQ ID NO:6), OB-Rd (SEQ ID NO:8), and OB-Re (SEQ ID NO:10), or allelic variants thereof;

b. a leptin receptor selected from the group consisting of:

i. N-terminal corresponding to OB-Ra through Lys⁸⁸⁹ and C-terminal corresponding to a C-terminal selected from the group consisting of OB-Rb after Lys⁸⁸⁹ (SEQ ID NO:86), OB-Rc after Lys⁸⁸⁹ (SEQ ID NO:87), and OB-Rd after Lys⁸⁸⁹ (SEQ ID NO:88);

ii. N-terminal corresponding to OB-Rb or OB-Rc through Lys⁸⁸⁹, and C-terminal corresponding to OB-Ra after Lys⁸⁸⁹ (SEQ ID NO:89,90) or OB-Rd after Lys⁸⁸⁹ (SEQ ID NO:91,92);

iii. N-terminal corresponding to OB-Rd through Lys⁸⁸⁹, and C-terminal corresponding to OB-Ra after Lys⁸⁸⁹ (SEQ ID NO:93), OB-Rb after Lys⁸⁸⁹ (SEQ ID NO:94), or OB-Rc after Lys⁸⁸⁹ (SEQ ID NO:95);

iv. N-terminal corresponding to SEQ ID NO:84 [55] from Pro⁶⁶⁴ to Lys⁸⁸⁹, and C-terminal corresponding to OB-Ra after Lys⁸⁸⁹ (SEQ ID NO:96), OB-Rb after Lys⁸⁸⁹ (SEQ ID NO:97), OB-Rc after Lys⁸⁸⁹ (SEQ ID NO:98), or OB-Rd after Lys⁸⁸⁹ (SEQ ID NO:99);

v. N-terminal corresponding to SEQ ID NO:84 [55] from Met⁷³³ to Lys⁸⁸⁹, and C-terminal corresponding to OB-Ra after Lys⁸⁸⁹ (SEQ ID NO:100), OB-Rb after Lys⁸⁸⁹ (SEQ ID NO:101), OB-Rc after Lys⁸⁸⁹ (SEQ ID NO:102), or OB-Rd

after Lys⁸⁸⁹ (SEQ ID NO:103);

vi. N-terminal selected from the group consisting of OB-Ra, OB-Rb, OB-Rd, and SEQ ID NO:84 [55] from Pro⁶⁶⁴ through His⁷⁹⁶, and OB-Re from His⁷⁹⁶ (SEQ ID NO:104,105,106 and 107); and

vii. N-terminal corresponding to SEQ ID NO:84 [55] from Met⁷³³ to His⁷⁹⁶, and OB-Re from His⁷⁹⁶ (SEQ ID NO:108);

c. a leptin receptor wherein

i. the N-terminal sequence is selected from the group consisting of

- (1) amino acid residues 1-889 (SEQ ID NO:109);
- (2) amino acid residues 23-889 (SEQ ID NO:110);
- (3) amino acid residues 28-889 (SEQ ID NO:111);
- (4) amino acid residues 133-889 (SEQ ID NO:112);
- (5) amino acid residues 733-889 (SEQ ID NO:113);
- (6) amino acid residues 1-796 (SEQ ID NO:114);
- (7) amino acid residues 23-796 (SEQ ID NO:115);
- (8) amino acid residues 28-796 (SEQ ID NO:116);
- (9) amino acid residues 28-796 preceded by an N-terminal Asp-Pro dipeptide (SEQ ID NO:117);
- (10) amino acid residues 133-796 (SEQ ID NO:118); and
- (11) amino acid residues 733-796 (SEQ ID NO:119); and

ii. the C-terminal sequence is selected from the group consisting of

- (1) SEQ ID NO:11;
- (2) SEQ ID NO:12;
- (3) SEQ ID NO:13;
- (4) SEQ ID NO:14; and
- (5) SEQ ID NO:15 after His⁷⁹⁶ (SEQ ID NO:120);

d. a leptin receptor having an amino acid sequence selected from the group consisting of

- i. Asp-Arg-Trp-Gly-Ser-Tyr⁴²⁰ (SEQ ID NO:77)--> Pro⁶⁴¹ (SEQ ID NO:121,122);
- ii. Asp-Arg-Trp-Gly-Ser-Ser¹¹⁸ (SEQ ID NO:78)--> Pro⁶⁴¹ (SEQ ID NO:123,124);
- iii. Asp-Arg-Trp-Gly-Ser-Leu¹²³ (SEQ ID NO:79) --> Val³³¹ (SEQ ID NO:125,126); and

e. a leptin receptor as described in (a)-(d) above in which a cysteine is substituted with an amino acid selected from the group consisting of serine, threonine, and alanine;

wherein the numbering is based on the amino acid sequence of SEQ ID NO:84 [55].

67. (Amended) A method for diagnosing body weight abnormalities in a mammal comprising detecting splice variants of OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of OB-R with an oligonucleotide hybridizable under stringent conditions to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of:

a. a leptin receptor selected from the group consisting of OB-Ra (SEQ ID NO:2), OB-Rb (SEQ ID NO:4), OB-Rc (SEQ ID NO:6), OB-Rd (SEQ ID NO:8), and OB-Re (SEQ ID NO:10), or allelic variants thereof;

b. a leptin receptor selected from the group consisting of:

i. N-terminal corresponding to OB-Ra through Lys⁸⁸⁹ and C-terminal corresponding to a C-terminal selected from the group consisting of OB-Rb after Lys⁸⁸⁹ (SEQ ID NO:86), OB-Rc after Lys⁸⁸⁹ (SEQ ID NO:87), and OB-Rd after Lys⁸⁸⁹ (SEQ ID NO:88);

ii. N-terminal corresponding to OB-Rb or OB-Rc through Lys⁸⁸⁹, and C-terminal corresponding to OB-Ra after Lys⁸⁸⁹ (SEQ ID NO:89,90) or OB-Rd after Lys⁸⁸⁹ (SEQ ID NO:91,92);

iii. N-terminal corresponding to OB-Rd through Lys⁸⁸⁹, and C-terminal corresponding to OB-Ra after Lys⁸⁸⁹ (SEQ ID NO:93), OB-Rb after Lys⁸⁸⁹ (SEQ ID NO:94), or OB-Rc after Lys⁸⁸⁹ (SEQ ID NO:95);

iv. N-terminal corresponding to SEQ ID NO:84 [55] from Pro⁶⁶⁴ to Lys⁸⁸⁹, and C-terminal corresponding to OB-Ra after Lys⁸⁸⁹ (SEQ ID NO:96), OB-Rb after Lys⁸⁸⁹ (SEQ ID NO:97), OB-Rc after Lys⁸⁸⁹ (SEQ ID NO:98), or OB-Rd after Lys⁸⁸⁹ (SEQ ID NO:99);

v. N-terminal corresponding to SEQ ID NO:84 [55] from Met⁷³³ to Lys⁸⁸⁹, and C-terminal corresponding to OB-Ra after Lys⁸⁸⁹ (SEQ ID NO:100), OB-Rb after Lys⁸⁸⁹ (SEQ ID NO:101), OB-Rc after Lys⁸⁸⁹ (SEQ ID NO:102), or OB-Rd after Lys⁸⁸⁹ (SEQ ID NO:103);

vi. N-terminal selected from the group consisting of OB-Ra, OB-Rb, OB-Rd, and SEQ ID NO:84 [55] from Pro⁶⁶⁴ through His⁷⁹⁶, and OB-Re from His⁷⁹⁶ (SEQ ID NO:104,105,106 and 107); and

vii. N-terminal corresponding to SEQ ID NO:84 [55] from Met⁷³³ to His⁷⁹⁶, and OB-Re from His⁷⁹⁶ (SEQ ID NO:108);

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 - (3) amino acid residues 28-889 (SEQ ID NO:111);
 - (4) amino acid residues 133-889 (SEQ ID NO:112);
 - (5) amino acid residues 733-889 (SEQ ID NO:113);
 - (6) amino acid residues 1-796 (SEQ ID NO:114);
 - (7) amino acid residues 23-796 (SEQ ID NO:115);
 - (8) amino acid residues 28-796 (SEQ ID NO:116);
 - (9) amino acid residues 28-796 preceded by an N-terminal Asp-Pro dipeptide (SEQ ID NO:117);
 - (10) amino acid residues 133-796 (SEQ ID NO:118); and
 - (11) amino acid residues 733-796 (SEQ ID NO:119); and

- ii. the C-terminal sequence is selected from the group consisting of

- (1) SEQ ID NO:11;
- (2) SEQ ID NO:12;
- (3) SEQ ID NO:13;
- (4) SEQ ID NO:14; and
- (5) SEQ ID NO:15 after His⁷⁹⁶ (SEQ ID NO:120);

- d. a leptin receptor having an amino acid sequence selected from the group consisting of

- i. Asp-Arg-Trp-Gly-Ser-Tyr⁴²⁰ (SEQ ID NO:77)--> Pro⁶⁴¹ (SEQ ID NO:121,122);
- ii. Asp-Arg-Trp-Gly-Ser-Ser¹¹⁸ (SEQ ID NO:78)--> Pro⁶⁴¹ (SEQ ID NO:123,124);

iii. Asp-Arg-Trp-Gly-Ser-Leu¹²³ (SEQ ID NO:79) -->Val³³¹ (SEQ ID NO:125,126); and

e. a leptin receptor as described in (a)-(d) above in which a cysteine is substituted with an amino acid selected from the group consisting of serine, threonine, and alanine;

wherein the numbering is based on the amino acid sequence of SEQ ID NO:84 [55].

69. (Amended) A method for measuring the expression of splice variants of OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of OB-R with a oligonucleotide hybridizable under stringent conditions to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of:

a. a leptin receptor selected from the group consisting of OB-Ra (SEQ ID NO:2), OB-Rb (SEQ ID NO:4), OB-Rc (SEQ ID NO:6), OB-Rd (SEQ ID NO:8), and OB-Re (SEQ ID NO:10), or allelic variants thereof;

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vi. N-terminal selected from the group consisting of OB-Ra, OB-Rb, OB-Rd, and SEQ ID NO:84 [55] from Pro⁶⁶⁴ through His⁷⁹⁶, and OB-Re from His⁷⁹⁶ (SEQ ID NO:104,105,106 and 107); and

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- (1) SEQ ID NO:11;
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